Innovative Treatment of Peripheral Nerve Injuries

Combined Reconstructive Concepts

Ivica Ducic, MD, PhD, Rose Fu, BS, and Matthew L. Iorio, MD

Background: Although autografts are the gold standard for failed primary nerve repairs, they result in donor-site morbidity. Nerve conduits and decellularized allografts are a novel solution for improved functional outcomes and decreased donor-site morbidity. Unfortunately, previous reconstructive algorithms have not included the use of decellularized allograft nerve segments, either for repair of the primary injury or reconstruction of the autograft donor site. To identify the optimal sequence of techniques and resources, we reviewed our cases of upper extremity peripheral nerve reconstruction.

Methods: A retrospective review was performed on consecutive patients who underwent upper extremity nerve reconstruction between August 2003 and September 2009. Outcomes were evaluated with the QuickDASH (disabilities of the arm, shoulder, and hand) questionnaire. Grouped outcome results were evaluated with analysis of variance analysis. A literature review of available options for nerve reconstruction was performed.

Results: In all, 47 patients were identified. Complete demographic/injury data were obtained in 41 patients with 54 discrete nerve repairs: 8 were repaired primarily, 27 with nerve conduits, 8 with allografts, and 11 with autografts. Time from injury to repair averaged 22.3 ± 38.3 weeks, with 12 repairs occurring immediately after tumor resection. Average QuickDASH score was 23.2 ± 19.8. An analysis of variance between repair-type outcomes revealed a P value of 0.58, indicating no outcome difference when each repair was applied for an appropriate gap. No comparable algorithm was identified in the literature analyzing the use of allograft in conjunction with conduit and autografts.

Conclusion: To restore maximal target-organ function with minimal donor-site morbidity, we have created an algorithm based on evidence for nerve reconstruction using allograft, conduit, and autologous donor nerve. Based on our clinical outcomes, despite small sample study, the adoption of the proposed algorithm may help provide uniform outcomes for a given technique, with minimal patient morbidity. Individualized reconstructive technique, based not only on nerve gap size but also on functional importance and the anatomical level of the nerve injury are important variables to consider for optimal outcome.

Key Words: peripheral nerve, allograft, nerve conduit, nerve graft

(*Ann Plast Surg* 2012;68: 180–187)

The treatment of peripheral nerve injuries is complicated by the disparate mechanisms of trauma, patient presentation, and any secondary bone or soft-tissue damages. To provide uniformly successful reconstructive outcomes in these settings, the goals of a tension-free and timely repair are paramount.[1] A tension-free primary repair is typically regarded as the optimal solution for a functional outcome, though this is not often possible as the mechanism of injury frequently requires debridement of crush or traction injury damage.[2] Small biomechanical accommodations can be performed to decrease the tension at the repair site, such as extended external neurolysis or a slight flexion/extension posture of a proximal joint; but, these maneuvers can further compromise the repair if postoperative contractures occur.[3] In those instances, primary repair cannot be obtained, and a multitude of existing reconstructive options need to be considered.

In addition to the current armamentarium of nerve conduits and autografts for sensory, or infrequently, motor nerves, as depicted in Figure 1, current novel reconstructive techniques include allograft nerve segments.[4] Allografts have demonstrated utility in large caliber defects, and they have the added benefit of no donor-site morbidity, though their use may be limited by a financial cost if they are not used judiciously and in the appropriate setting. Conversely, autografts require the harvest of an otherwise healthy donor nerve, and there remains a risk of donor-site complications, including infection, postoperative paresthesias, or functional compromise. Further, third-party reimbursement rates may be seemingly based on disease-independent criteria, such as a repair without the need for an allograft or with minimal operative time. To address this concept, we have based our techniques principally on repairs with decreased patient morbidity and maximal functional outcome. Unfortunately, because of the varied techniques for nerve reconstruction, a unified algorithm for repair of peripheral nerve defects is currently difficult to identify in the literature.

Based on this premise, we hypothesized that an evidence-based algorithm of long-term outcomes would be optimized by a focus on functional importance and defect size. To identify the optimal sequence of techniques and resources, we reviewed our cases of upper extremity nerve reconstruction and evaluated the patient morbidity and functional outcomes using such an algorithm.

METHODS

Following institutional review board approval, a retrospective review was performed on all consecutive patients who presented for any upper extremity nerve repair between August 2003 and September 2009. Patient demographic information, including age, sex, injury mechanism, and time to follow-up, was recorded. All patients were evaluated and treated by a single surgeon (I.D.). Patients were then contacted for a subsequent postoperative follow-up and outcome evaluations. A previously validated outcomes tool, the QuickDASH survey, was administered to all patients who consented for involvement in the study.

The QuickDASH (disabilities of the arm, shoulder, and hand) questionnaire is a validated tool based on the patient's perception of pain and functional impairment, and a normative value in a noninjured population is 10.10 ± 14.68 of 100 points, with a lower score

---

Received June 16, 2011, and accepted for publication, after revision, September 5, 2011.

From the Department of Plastic Surgery, Georgetown University Hospital, Washington, DC.

Presented at the Northeastern Society of Plastic Surgeons Annual Meeting, October 2010, Washington, DC.

Conflicts of interest and sources of funding: none declared.

Reprints: Ivica Ducic, MD, PhD, Department of Plastic Surgery, Peripheral Nerve Surgery Institute, Georgetown University Hospital, 3800 Reservoir Road NW, Washington, DC 20007. E-mail: ducici@gunet.georgetown.edu.

ISSN: 0148-7043/12/6802-0180
DOI: 10.1097/SAP.0b013e3182361b23

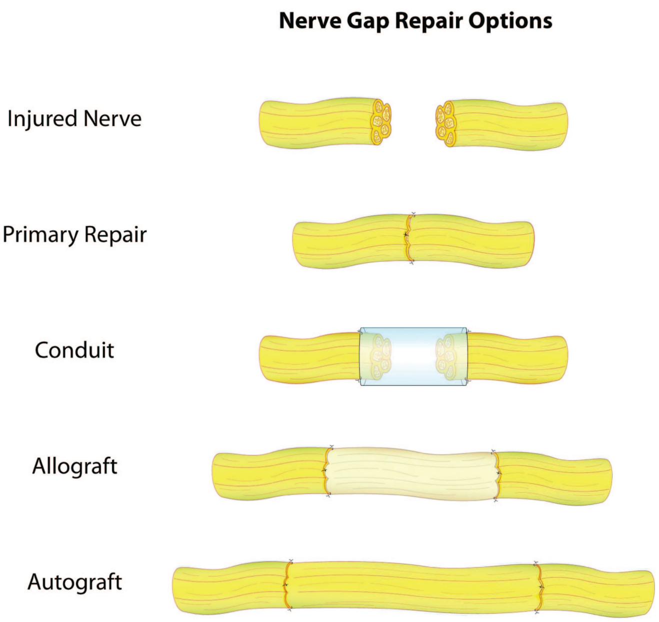


FIGURE 1. Peripheral nerve gap repair options.

denoting minimal disability.[5] The survey has a high internal consistency and validity rating for maintaining individual patient evaluations.[6,7] This was completed retrospectively as a final follow-up visit and was independently administered by 1 consistent practitioner/author other than the operating surgeon.

Patients were excluded if they were unable to reach for follow-up, complete chart and demographic data could not be verified, or were unable to consent for involvement in the study. In addition, patients with secondary or tertiary reconstructions or operative sites with preoperative active infections were excluded from the study. It was hypothesized that a comparison of continuous outcome results among allograft, conduit, and autograft would demonstrate no differences when each treatment modality is used for a congruent functional application and defect size. To determine this, grouped results were evaluated using a 1-way analysis of variance test within the proposed algorithm. In addition, a literature review of available options for nerve reconstruction was performed.

Surgical Technique

We have previously adopted an outcome-based treatment algorithm and have implemented the use of allografts in an effort to improve our reconstructive techniques. Figure 2 demonstrates our algorithm for peripheral nerve reconstruction. This approach has allowed us to simplify our management of these injuries by using a composite of repair techniques that are principally centered on defect size and the functional importance of the reconstructed nerve.

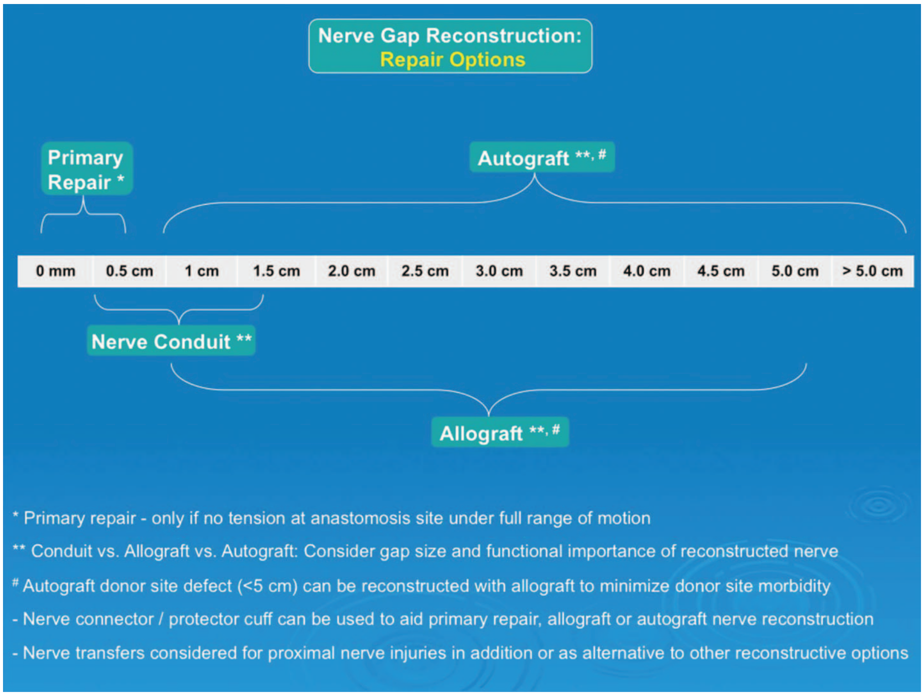
Primary nerve repair is performed with appropriate size (micro)sutures, tissue glues, or with available nerve connectors only if a tension-free repair is observed intraoperatively by taking the extremity through the maximal range of motion. It is our observation that only a minimal percentage of patients in our practice qualify for a primary repair, given the cases of extensive nerve damage with a chronic injury that present as consults in the outpatient setting. When possible, it is the author's preference to repair the injury primarily and to use a 5-mm nerve connector (AxoGuard, AxoGen, Inc., Alachua, Florida) over the anastomosis. As depicted in Figure 3, this allows a controlled and optimal opposition of the reconstructing fibers, a minimization of axonal wasting with collateral sprouting or possible fiber misalignment/neuroma formation, all of which should potentially optimize the outcome.[8] We find this particularly useful in smaller but polyfascicular nerves where proper fascicular opposition can be rather challenging and time-consuming without connector use.

The differentiation between primary repair without tension and a minimal gap requiring interposition conduit/graft varies from nerve to nerve and site to site, depending on mobility intrinsic to the nerve location, caliber, and injury. In addition, further variance can occur within the same nerve as a result of previous trauma or adjacent surgery in the nerve environment, making it potentially less mobile than expected and subsequently requiring an interposition conduit/graft instead of a primary repair. Intraoperative observation of nerve excursion under extremity flexion/extension and resultant repair site tension are critical to determine the true extent of the defect gap and appropriate repair technique. Considering this, we find that there is no absolute minimal gap size/number that can be used for primary repair, rather intraoperative clinical observation remains critical when determining proper type of the reconstruction.

Following resection of the proximal and distal ends of the injured nerve, gap size under maximal range of motion of proximal/distal joint and clinical importance of the nerve will then dictate the type of interposition conduit/graft to be used. Conduits have been reported in the literature for various gap sizes, even beyond 30 mm.[2] We initially limited their use for <15 mm of defects, and we have even further modified it presently when allografts are available. Although there are a number different nerve conduits available, our preference at this time is collagen (NeuraGen, Integra life Sciences, Plainsboro, NJ) or polyglycolic acid (NeuroTube, Synovis Life Technologies, Birmingham, AL), depending on the unique reconstructive goal and the surrounding tissue characteristics required. Again, it is imperative to ensure a tension-free repair as well as an appropriate fit of the nerve within the conduit ends. Figure 4 demonstrates 5-mm radial sensory nerve injury caused by knife reconstructed with a nerve conduit.

The third category includes readily available human nerve allografts (Avance, AxoGen, Inc., Alachua, FL), which may be indicated preferentially over nerve conduits, depending on the reconstructive goals required for the individual application. Based on studies performed by Whitlock et al for the repair of long nerve gap defects, decellularized allografts offer a scaffold for regenerating axons and incoming Schwann cells.[9] This may enhance the structural integrity of the construct as compared with conduit reconstructions and increase the regenerative ability of the damaged nerve. As the injured nerve is dependent on the architecture of the intrinsic laminin and substructure of the endoneurium during the repair, allograft appears to be a better choice when compared with conduits. In addition, allograft may also be used for a wider range of defects than conduit, especially if the nerve being reconstructed carries a critical function. It is the author's preference to again use a nerve connector over both the proximal and distal anastomosis sites for the same aforementioned reasons. Figure 5 demonstrates a traumatic injury resulting in a neuroma-in-continuity in radial digital nerve of the index finger and a reconstruction using allograft nerve and nerve connectors, whereas Figure 6 demonstrates a 4-cm nerve fascicle reconstruction following peripheral nerve tumor resection.

The fourth category for larger defects includes autograft nerve reconstruction. Applicable gap sizes can range depending on the functional importance of reconstructed nerve. In the setting of autograft harvest, we prefer to use allograft to backgraft the donor site in an effort to minimize functional morbidity, especially in the case of motor nerve harvests. In such cases, up to 5 cm (at the present time) of harvested donor nerve can be reconstructed with allograft to minimize donor-site morbidity. Again, all repairs are protected with a 5-mm nerve connector to minimize collateral



* Primary repair - only if no tension at anastomosis site under full range of motion

** Conduit vs. Allograft vs. Autograft: Consider gap size and functional importance of reconstructed nerve

\# Autograft donor site defect (<5 cm) can be reconstructed with allograft to minimize donor site morbidity

- Nerve connector / protector cuff can be used to aid primary repair, allograft or autograft nerve reconstruction
- Nerve transfers considered for proximal nerve injuries in addition or as alternative to other reconstructive options

FIGURE 2. Peripheral nerve reconstructive algorithm, differentiated by nerve defect characteristics and repair modality.

sprouting and functional axonal loss and to guard against a potential neuroma site.[8] Figure 7 demonstrates a 5-cm major peripheral nerve defect reconstruction following major peripheral nerve traumatic injury. Lastly, combination of available products can be considered to further aid nerve reconstructive options. Figure 8 demonstrates the use of nerve connectors and/or protector with allograft nerve reconstruction, as well as the nerve protector serving as a nerve wrap within scarred environment.

RESULTS

In all, 47 consecutive patients were identified, and full demographic and operative data were obtained in 41 patients with 54 discrete nerve repairs. Average age of the patients was 46.4 ± 17.5 years old, and the most common surgical indication was trauma (sharp/lacerating 20 repairs; crush 8 repairs; fracture 4 repairs; gunshot 2 repairs), followed by tumor (11 repairs), iatrogenic nerve injuries (7 repairs), and infection (2 repairs). Time from injury to repair was an average of 22.3 ± 38.3 weeks, with 12 repairs occurring immediately at the time of tumor resection. The frequency of each individual repair type is outlined in Table 1.

Of the 54 nerve repairs, primary tension-free repair was achieved in 8 repairs, 27 were completed using nerve conduits, 8 with nerve allografts, and 11 using harvested nerve autografts. Minimum follow-up was >2 years. Average QuickDASH score was 23.2 ± 19.8. An analysis of QuickDASH variance between repair types (analysis of variance) revealed a P value of 0.56, which was not a significant difference in QuickDASH outcomes. No complications of infection, dehiscence, or seroma were found in these study patients.

Our literature search identified isolated, cited studies concerning each of the 4 aforementioned reconstructive groups discussed, but no practical algorithm syncing them according to the defect size or functional nerve role.

DISCUSSION

The driving force for the treatment of peripheral nerve repairs is centered on a functional outcome. Multiple factors, however, can influence or retard the effectiveness of the treatment, including the mechanism of injury, where a crush or rupture/avulsion injury will suffer more diffuse damage and possibly larger intercalated defects as compared with a straight line laceration.[10] For this reason, resection of injured nerve to the level of healthy fascicles is critical for optimization of nerve regeneration.

The functional element of repair is also dependent on the timing sufficient to allow appropriate healing in cases of neuropraxia or minor axonotmesis and avoidance of further axonal disruption or motor end plate degeneration. A protracted course of nerve injury can result in a poor functional outcome due to chronically denervated Schwann cells as well as the loss of target motor end plates over time, as denervated muscle atrophies quickly and prolonged axonal deprivation will result in irreversible disability.[11] The optimal period for repair of a peripheral nerve injury is typically within

TABLE 1. Repair Type and Defect Interval and Characteristics of All Upper Extremity Peripheral Nerve Repairs (N = 54)

Repair Type	Number	Average Gap (mm)	Injury Duration (wk)	Average Follow-Up (wk)	QuickDASH
Primary repair	8	0/Tension free	27.9 + 52.9	204.0 ± 41.3	14 ± 1.3
Conduit repair	27	9.1 ± 3.7	25.9 ± 47.4	186.4 ± 56.7	33 ± 15.3
Allograft repair	8	17.6 ± 7.5	6.4 ± 5.2	129.7 ± 89.2	19.8 ± 10.4
Autograft repair	11	37.5 ± 13.2	10.4 ± 10.9	250.5 ± 59.3	22.5 ± 11.1

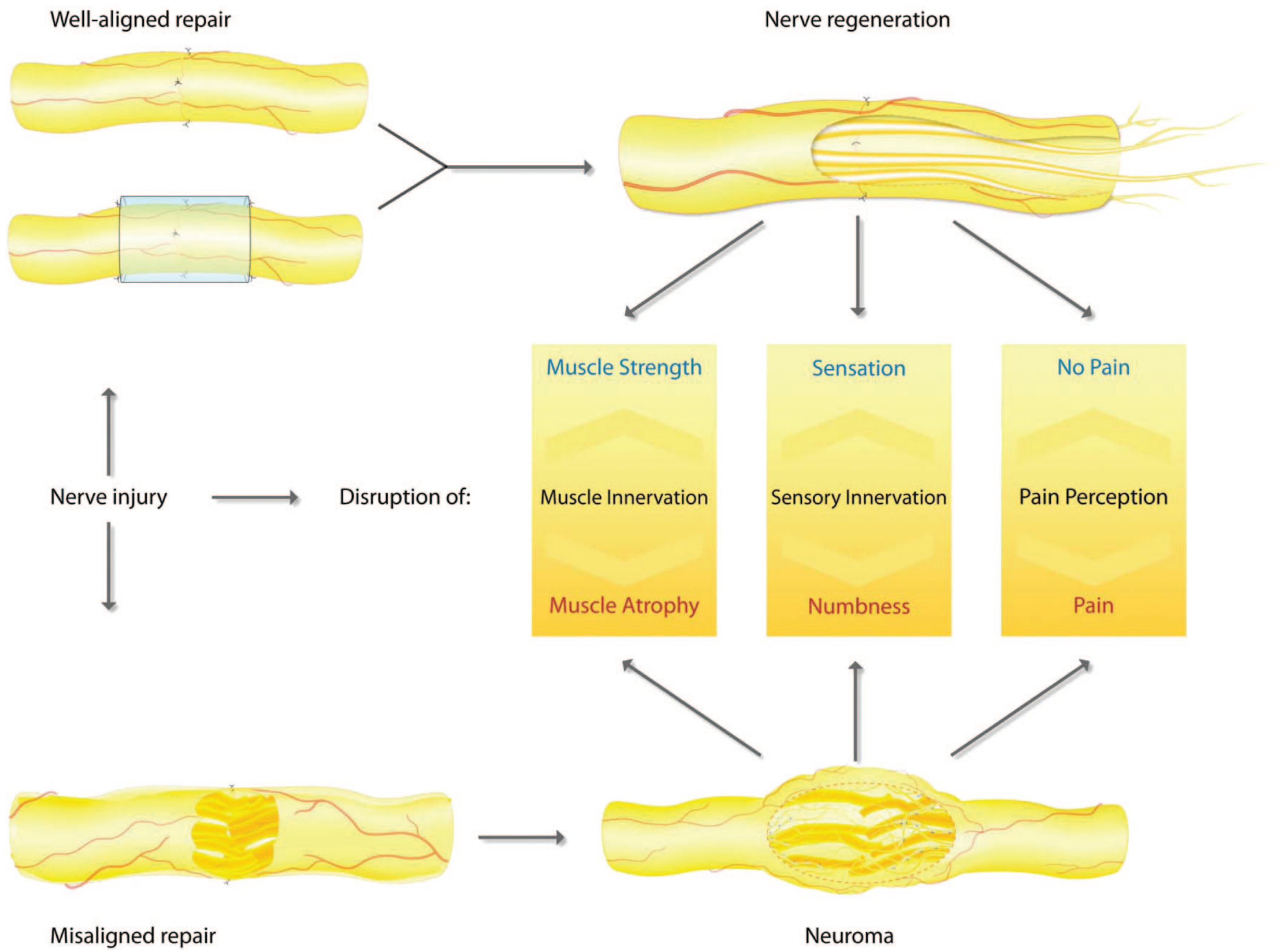


FIGURE 3. Peripheral nerve injury outcomes. With properly opposed nerve ends and aligned fascicles during primary repair, with or without a nerve connector, normal nerve regeneration across the repair site and thus optimal functional outcome can be expected. In the case of fascicle misalignment during primary repair, negative functional outcome labeled by pain or loss of functional recovery may result.

3 weeks, ideally immediately.[12] Thus, the longer the distance that nerve needs to travel when regenerating from injury site to the target organ, a less optimal functional recovery time can be expected.

In addition to the mechanism of injury, timing of the repair, and the regional nerve anatomy, adjacent potential anatomic nerve compression sites are other important variables to consider. Based on a "double-crush phenomena," if overlooked, distal nerve compression can negatively affect nerve regeneration, despite properly chosen nerve repair techniques.[13,14] Scheduled clinical follow-up after nerve repair can prospectively help detect these potential issues. When confirmed, they warrant timely nerve decompression at the adjacent/distant nerve anatomic compression sites to allow unobstructed nerve regeneration.

Once the diagnosis of a discontinuous nerve defect is verified, surgical therapy involves debridement of any nonviable nerve tissue and adjacent proximal and distal neurolysis to encourage a tensionless segment closure, when possible.[2] However, animal studies have demonstrated a severe decrease in neural blood flow, with minimal tension across the anastomotic site, where a 15% increase in nerve tension can produce a dramatic 80% decrease in blood flow and lead to irreversible ischemic damage and impaired nerve growth.[15] To circumvent this, early repair techniques used bone shortening or joint immobilization, frequently in a flexed position, to decrease the resting tension on the proximal nerve segment. Although this may in fact allow for a "tension-free" primary repair, the subsequent joint contracture and loss of mobility are preclusive to the overall rehabilitative effort. Therefore, as minimal tension is required to decrease neurovascular perfusion at the repair site, alternative techniques to primary repair should be performed if any tension is apparent following full range of motion at the proximal and distal joints of the injury.

Classically considered the gold standard for reconstruction, autografts have been cited in multiple studies outlining their utility in both large and small nerve defect repairs, as autografts have the advantage of transferring native Schwann cells to the regenerating defect, which may provide the scaffold for nerve regeneration.[16] This technique, however, is not without its own sequelae, as the nerve defect is effectively moved from one site to another. Autografting necessitates the harvest of a donor nerve that can result in significant donor-site morbidity such as sensory paresthesias or postoperative neuroma formation, and the grafts are limited by an

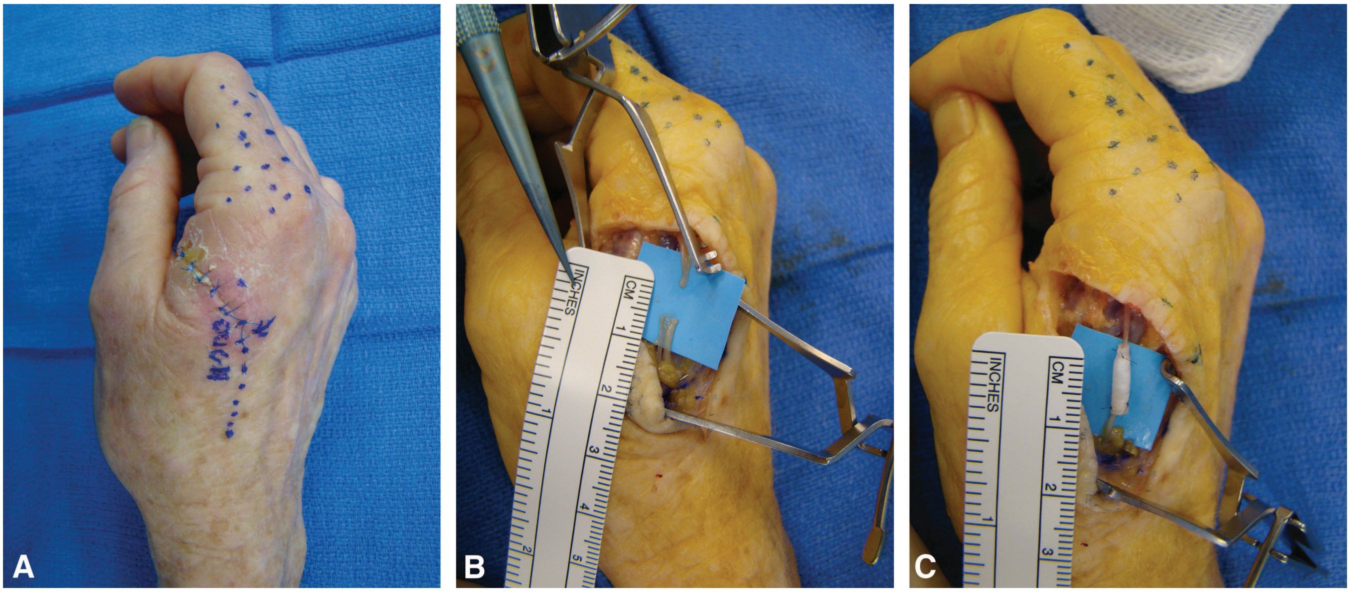


FIGURE 4. A, Traumatic injury to the radial sensory digital nerve in 65 year-old patient, resulting in pain at the injury site and finger numbness. B, Excision of pain-generating neuroma. C, Resulting 5 mm gap reconstructed with nerve conduit.

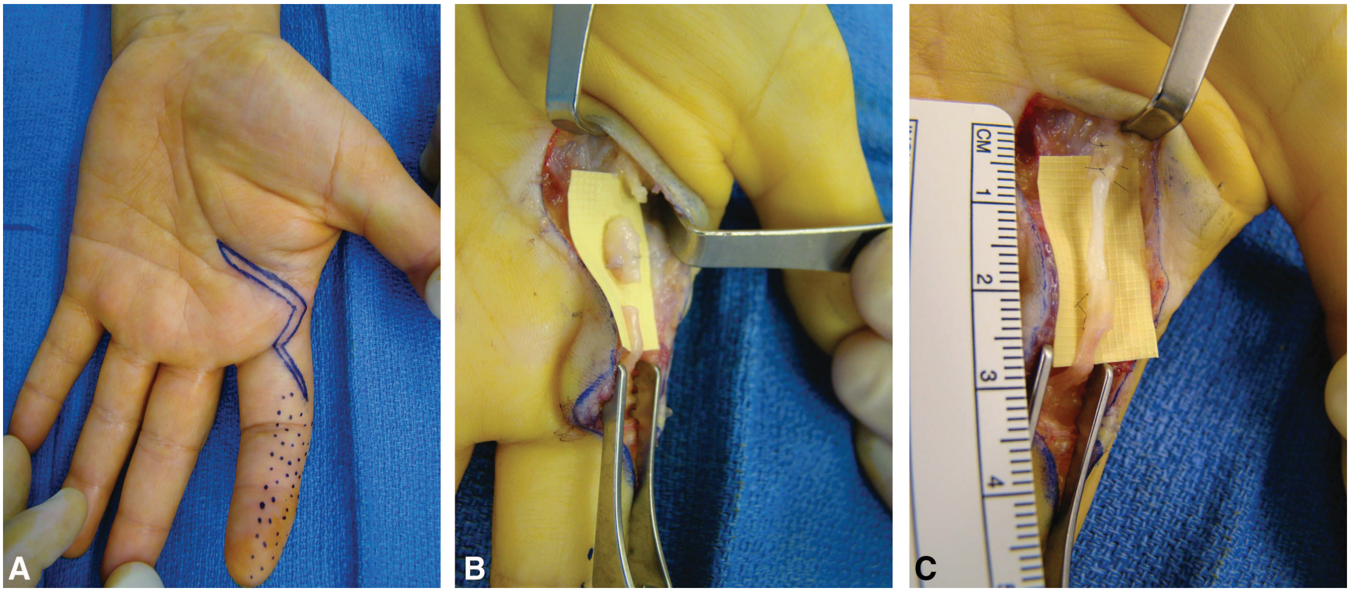


FIGURE 5. A, Knife injury to hand in a 37 year-old patient, resulting in irregular scar, pain and finger numbness. B, Excision of neuroma-in-continuity of the index finger digital nerve. C, Reconstruction of 20 mm nerve defect to restore finger sensibility with nerve allograft and anastomotic nerve connector.

availability of sufficient length, caliber, and fascicle density in expendable nerve donor sites.[17] As demonstrated by Brushart et al in an experimental model of nerve growth influenced by motor or sensory nerve autografting, donor nerve function is a dominant function in growth selectivity.[18] An injured motor nerve was found to advance preferentially along a motor nerve autograft and similarly for a sensory nerve injury. Frequently, however, motor nerve grafts are precluded by a secondary loss of function or minimal donor length. In an effort to decrease the morbidity of autografting, several alternative options, including nerve conduits and allografts, have come to the forefront.

Conduits have been demonstrated in both animal and human models to provide an adequate scaffold for nerve reconstruction. By aiding in the directional growth or alignment of the fascicle growth cone, nerve regeneration has been demonstrated in defects as large as 30 mm.[19,20] In comparison with previously used vein grafts, the material remains intrinsically stented open in larger defect sizes, whereas vein grafts are known to collapse and contribute to subsequent scar formation.[20] In a multicenter, randomized, prospective trial, Weber et al compared nerve conduits with autografting for a range of peripheral nerve defect sizes and determined that conduits may in fact be more advantageous in small nerve gaps. In defects of

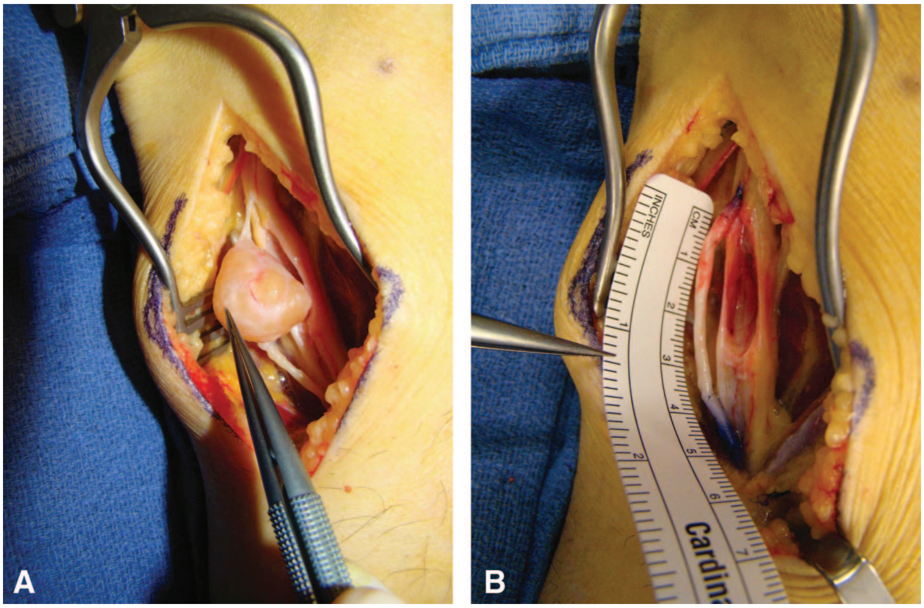


FIGURE 6. A, Peripheral nerve tumor requiring excision of associated fascicle. B, Reconstruction of 40 mm nerve fascicle defect with nerve allograft and anastomotic nerve connector.

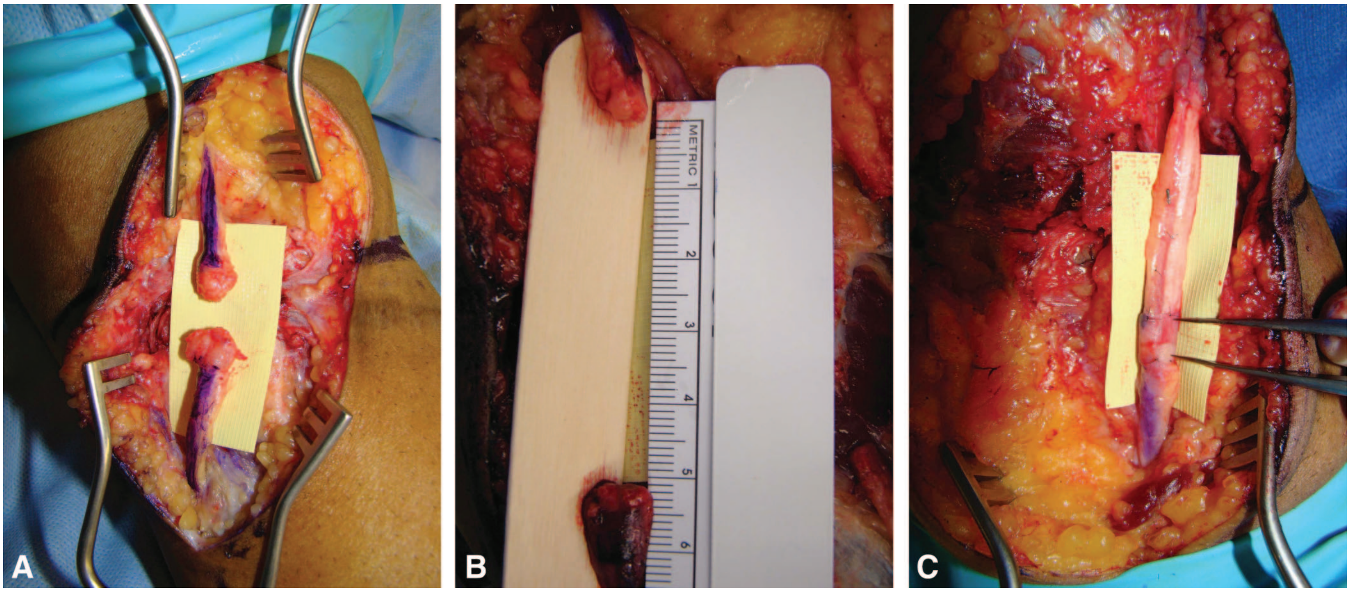


FIGURE 7. A, Traumatic injury to a major peripheral nerve in a 25 year-old patient. B, Final defect size after stump debridement to healthy fascicular tissue. C, Reconstruction of 50 mm nerve defect with sural nerve autograft. (Donor medial and lateral sural nerve defect reconstructed with 50 mm nerve allograft and anastomotic nerve connector.)

similar size to the conduit group in our algorithm, the conduit group had significantly superior moving 2-point discrimination than the control group (3.7 ± 1.4 mm to 6.1 ± 3.3 mm, $P = 0.02$). Additionally, the results were not significantly different between conduit versus primary repair in a midrange of gap sizes, with an average moving 2-point discrimination of 8.9 ± 4.1 mm in the conduit group and 6.0 ± 3.7 mm in the control group ($P = 0.12$). Similar results have been echoed in subsequent studies. A prospective, multicenter, randomized trial performed by Bertleff et al followed 34 digital nerve lacerations in 30 patients randomized to receive either standard repair or repair with a nerve conduit.[21] Following repair, the results did not vary significantly between the 2 groups, as measured by moving and static 2-point discrimination. Lastly, Bushnell et al published a follow-up of conduit repairs, in 10- to 12-mm defects, with an average follow-up of 15 months and demonstrated an average score of 10.86 mm.[22]

However, as the functional demand of the injured nerve or the defect size enlarges, conduits perform less optimally, and may be preferentially replaced by allografts as a viable reconstructive option.[4,9,23] Cadaveric allografts enable restoration of nerve continuity after injury and provide a scaffold upon which host nerve regeneration can occur. Allograft nerve segments, though not a new technology, were previously a morbid reconstructive option because of the need for temporary patient immune suppression, as early allograft segments contained allogeneic Schwann cells and cellular material. As such, these donor segments were difficult to incorporate

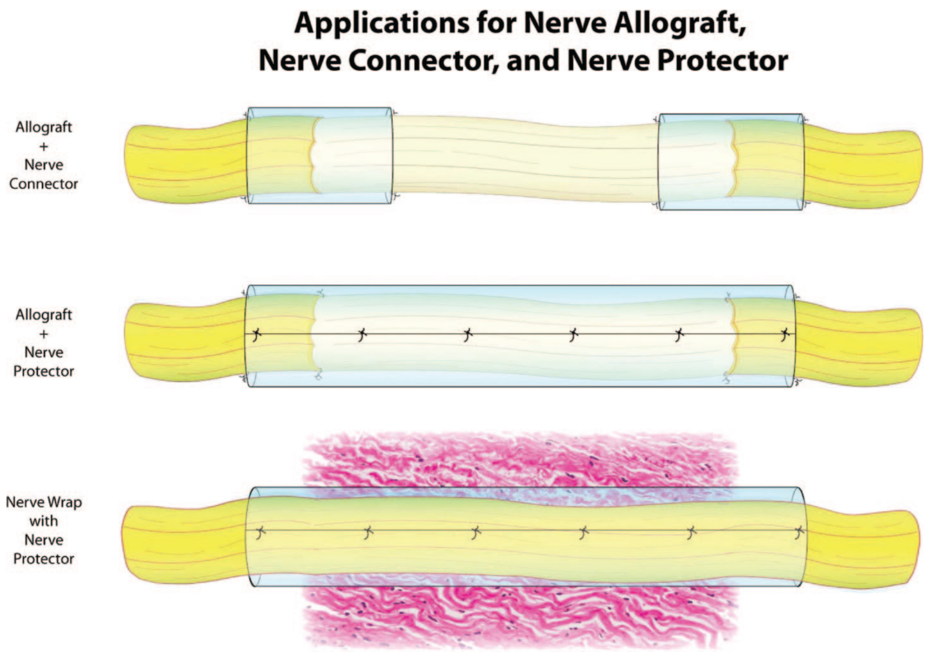


FIGURE 8. Applications for the use of nerve connector and protector with allograft nerve reconstruction. Nerve wrap with nerve protector used to minimize scarring of the exposed or decompressed nerve, especially if within scarred surroundings.

into a universal algorithm for reconstruction. Newer preparations use improved technology with cold processing for antigenic Schwann cell processing and removal, the need for immune suppression, and its attendant complications are obviated.[10,20] The benefits of the allograft remain the same, however, with excellent functional outcomes associated with the retained nerve architecture. Host Schwann cells repopulate the allografts, and thereby use it as a scaffold for bridging the defect, with an eventual resorption of the allograft material. Given the relative antigenic neutrality of the allograft, a restoration of protective sensation or function may additionally be regained when used to restore continuity of an autograft harvest site, or when a multifocal defect requires multiple grafts, thereby decreasing the overall morbidity of the index operation. Allografting may be an optimal solution for reconstruction in large caliber or functionally dependent injuries that either require multiple sites of graft or are limited by autografting availability or morbidity. Although allograft benefits when reconstruction sensory vs. motor nerves will be even further defined in the near future, its role as interposing (allo)graft for supercharging nerve transfers is already applied in clinical practice.

Our study was limited by similar bias shared by other retrospective studies, including a small study population and recall bias. In addition, the analysis was based on the supposition that varying methods of reconstructive techniques are used in similarly appropriate surgical methods, and that the functional and sensory outcomes in the literature are indeed valid. It is important to note that our study was not about proving one approach better than another, rather each discussed reconstructive modality has its role, achieving functional outcomes when applied in the proper setting. In addition, as depicted in Figure 2, our proposed algorithm, unlike others available, summarizes all available reconstructive options to date for nerve injuries at a given anatomic gap. It is suggested that primary repair be used only if no tension at the repair site is noted under full range of motion of reconstructed extremity/body part. Despite nerve conduits initially used for defects up to or even beyond 3 cm, based on new data presented by Whitlock et al, we have modified our algorithm currently by reserving nerve conduits for very small defects, usually up to 1 cm. Another modification worth noting, based on clinical and experimental data available, is concerning nerve allografts applied for defects up to 5 cm. Although current published data are available for 3 cm defects or less, new ongoing clinical research is suggesting safe use up to at least 5 cm gaps. Brooks recently presented data where functional recovery reported for 30- to 50-mm defects was 88%, whereas it was 85% for 15- to 29-mm defects and 100% for 5- to 14-mm defects (n = 26, 34, and 16, respectively).[24] Although we noted similar recovery responses in our study, these very encouraging results will certainly be further examined in new prospective multicenter studies, especially addressing 30 to 50 mm or more gaps.

Considering that central to the treatment of these injuries is an appropriate identification of the functional workload of the affected nerve, for defects larger than 5 cm, or for restoration of functionally critical motor nerve function of any size, at this time, we prefer autografts, given they still offer the best regeneration. If autografts harvest created <5-cm donor-site defects, we suggest its reconstruction with allograft to minimize if not eliminate donor-site nerve morbidity. Lastly, as the final decision which of the aforementioned options will best suit an individual patient's needs, in a nerve injury that is proximal enough to compromise meaningful recovery, functional nerve transfers might need to be considered as well.[25]

CONCLUSIONS

The treatment of peripheral nerve injuries is complicated by varying degrees of injury severity, functional impact, and the lack of consensus on repair modalities given new reconstructive choices. Based on our clinical outcomes, and those in the available literature, if an algorithm of repair is driven by defect size and functional goals are adopted to guide the use of nerve conduit, allograft and autograft reconstructions, it may be possible to provide uniform patient outcomes with minimal functional or surgical morbidity. The addition of allograft to the reconstructive armamentarium appears to decrease and prevent autograft morbidity, with equivalent patient functional outcomes for appropriate nerve defect size. We hope that prospective, multicenter studies on a larger population can prove and further define the algorithm we have proposed.

REFERENCES

1. Hart AM, Terenghi G, Wiberg M. Neuronal death after peripheral nerve injury and experimental strategies for neuroprotection. *Neurol Res*. 2008;30: 999–1011.
2. Strauch B. Use of nerve conduits in peripheral nerve repair. *Hand Clin*. 2000;16:123–130.
3. Terzis J, Faibisoff B, Williams B. The nerve gap: suture under tension vs. graft. *Plast Reconstr Surg*. 1975;56:166–170.
4. Karabekmez FE, Duymaz A, Moran SL. Early clinical outcomes with the use of decellularized nerve allograft for repair of sensory defects within the hand. *Hand*. 2009;4:245–249.
5. Hunsaker FG, Cioffi DA, Amadio PC, et al. The American Academy of Orthopaedic Surgeons Outcomes Instruments—normative values from the general population. *J Bone Joint Surg*. 2002;84A:208–215.
6. Beaton DE, Katz JN, Fossel AH, et al. Measuring the whole or the parts? Validity, reliability, and responsiveness of the disabilities of the arm, shoulder, and hand outcome measure in different regions of the upper extremity. *J Hand Ther*. 2001;14:128–146.
7. Gummeson C, Ward MM, Atroshi I. The shortened Disabilities of the Arm, Shoulder, and Hand Questionnaire (QuickDASH): validity and reliability based on responses within the full-length DASH. *BMC Musculoskelet Disord*. 2006;7:44.
8. Krarup C, Archibald SJ, Madison RD. Factors that influence peripheral nerve regeneration: an electrophysiological study of the monkey median nerve. *Ann Neurol*. 2002;51:69–81.
9. Whitlock EL, Tuffaha SH, Luciano JP, et al. Processed allografts and type I collagen conduits for repair of peripheral nerve gaps. *Muscle Nerve*. 2009; 39:787–799.
10. Isaacs J. Treatment of acute peripheral nerve injuries: current concepts. *J Hand Surg Am*. 2010;35:491–497.
11. Nath RK, Mackinnon SE. Nerve transfers in the upper extremity. *Hand Clin*. 2000;16:131–139.
12. Kobayashi J, Mackinnon SE, Watanabe O, et al. The effect of duration of muscle denervation on functional recovery in the rat model. *Muscle Nerve*. 1997;20:858–866.
13. Upton AR, McComas AJ. The double crush in nerve entrapment syndromes. *Lancet*. 1973;2:359–362.
14. Mackinnon SE, Dellon AL. Multiple crush syndrome. In: Mackinnon SE, ed. *Surgery of the Peripheral Nerve*. 1st ed. New York, NY: Thieme Medical Publishers; 1988:347–392.
15. Clark WL, Trumble TE, Swiontkowski MF, et al. Nerve tension and blood flow in a rat model of immediate and delayed repairs. *J Hand Surg*. 1992;17A:677–687.
16. Wilgis EFS. Nerve repair and grafting. In: Green DP, ed. *Operative Hand Surgery*. Vol 2. 2nd ed. New York, NY: Churchill Livingstone; 1988:1373–1404.
17. Millesi H. Techniques for nerve grafting. *Hand Clin*. 2000;16:73–91.
18. Brushart TM, Seiler WA. Selective reinnervation of distal motor stumps by peripheral motor axons. *Exp Neurol*. 1987;97:289–300.
19. Mackinnon SE, Dellon AL. Clinical nerve reconstruction with bioabsorbable polyglycolic acid tube. *Plast Reconstr Surg*. 1990;85:419.
20. Weber RA, Breidenbach WC, Brown RE, et al. A randomized prospective study of polyglycolic acid conduits for digital nerve reconstruction in humans. *Plast Reconstr Surg*. 2000;106:1036–1045.
21. Bertleff M, Meek MF, Nicolai JP. A prospective clinical evaluation of biodegradable Neurolac nerve guides for sensory nerve repair in the hand. *J Hand Surg*. 2005;30A:513–518.
22. Bushnell BD, McWilliams AD, Whitener GB, et al. Early clinical experience with collagen nerve tubes in digital nerve repair. *J Hand Surg*. 2008;33A: 1080–1087.
23. Belkas JS, Choichet MS, Midha R. Peripheral nerve regeneration through guidance tubes. *Neurol Res*. 2004;26:151–160.
24. Brooks D. A multicenter retrospective study of processed nerve allograft evaluating utilization and outcomes in peripheral nerve injury repair, upper extremity cohort analysis (RANGER). Paper presented at: 2010 American Society for Surgery of the Hand; October 7–9, 2010; Boston, MA.
25. Mackinnon SE, Novak CB. Nerve transfers. New options for reconstruction following nerve injury. *Hand Clin*. 1999;15:643–666.